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Compliance with Results Reporting at ClinicalTrials.gov Before and After the 2017 FDAAA Final Rule: A Comparative Analysis

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Abstract

Background: Federal rules clarifying clinical trial reporting requirements took effect in 2017, implementing Section 801 of the Food and Drug Administration Amendments Act (FDAAA) of 2007 with penalties for noncompliance. This study examines how reporting rates changed after these regulations across different trial types, funding sources, and other characteristics.

Methods: This analysis compared FDAAA-mandated trial reporting compliance across two windows: 2010–2014 completions (Window 1) and 2017–2021 completions (Window 2), tracking each trial's reporting status for 3 years post-completion. The study evaluated 12-month reporting compliance rates between windows and analyzed patterns across trial characteristics. Analyses were conducted both with and without consideration of regulatory reporting extensions.

Results: We identified 14,174 HLACTs in Window 1 (2010–2014) and 9,880 HLACTs in Window 2 (2017–2021) with completion dates on either side of the January 18th, 2017 rule effective date. Twelve-month reporting rates increased from 8.3% to 23.2% (+14.9%) while 36-month rates increased from 40.8% to 49.2% (+8.5%). Improvements in rates occurred across all trial characteristics (funding source, trialphase, intervention type, and trial purpose). While Anderson et. al.'s study found NIH-funded trials lagging behind industry trials, post-2017 rates became similar with NIH and industry at 32.2%/31.5% within 12 months and 62.0%/67.1% within 36 months respectively.

Conclusion: Overall, across all trials and all sub-categories, we observe improvements in compliance rates after the 2017 mandate, particularly among NIH-funded trials. However, although compliance has improved, a consistent majority remains out of compliance with 76.8% of post-mandate trials not reporting within 12 months and 50.8% not reporting within 36 months. These persistent low rates suggest that additional policy measures or structural changes may be needed to achieve the transparency goals of the FDAAA Section 801. Understanding and addressing the barriers to timely reporting remains critical for advancing public health and medical research.

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1 - Background

Historically, results from clinical trials involving human experimentation have been withheld from public view, raising concerns about transparency in clinical research. To address this, in 2000, Congress established the registry ClinicalTrials.gov, operated by the National Library of Medicine (NLM) of the National Institutes of Health (NIH).[1]

Subsequently, the Food and Drug Administration Amendments Act of 2007 (FDAAA) Section 801[2] mandated that applicable clinical trials (ACTs) must submit their summary results to the ClinicalTrials.gov data-bank one year from study completion. This regulation went into effect under the "Final Rule" on January 18, 2017 and compliance was required from April 18, 2017 for all responsible parties.[3,4,5,6] Penalties for non-compliance include fines, loss of federal funding, and public disclosure of non-compliance.

Previous work by Anderson et al.[7] examined the ClinicalTrials.gov database between the2007 reporting requirement and the 2017 "Final Rule." They found that only 13.4% of applicable trials reported results within the required 12-month window after trial completion. Similarly, Riley et al.'s[8] analysis of pulmonary trials during this period found a 15% compliance rate.[8]

DeVito et al.[9] conducted the first evaluation of compliance after the Final Rule implementation, examining trials from 2017. They reported a 40.9% compliance rate for results reporting within the one-year deadline.[9] While DeVito's study used a more flexible approach to assessing compliance (accounting for trial extensions and other permissive modifications), the present study employs a more direct interpretation of the policy requirements and accounts for extensions in the provided supplement. This analysis extends previous work substantially by examining trials completed through 2021, providing a longer four-year window after the Final Rule implementation.

Seven years after the FDAAA Final Rule's 2017 implementation, we seek to evaluate how compliance rates have changed.

2 - Methods

As there is no definitive way to determine which clinical trials were subject to FDAAA provisions, we followed the algorithm developed by Anderson et al.[7] to identify trials that are likely to be ACTs, which they term highly likely applicable clinical trials (HLACTs). The criteria for applicable trials in our sample include intervention trials of drugs, medical devices, or biologics in trial phase 2, 3, or 4, meeting criteria for FDA oversight (table 1).

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Table 1: Count of Trials by successive exclusion criteria for Window 1 (2010–2014, tracked until 2017) and Window 2 (2017–2021, tracked until 2024).

Window 1 Remaining	(Excluded)	Window 2 Remaining	(Excluded)	Criteria to Meet
234,668		**480,228**		**Trials registered with ClinicalTrials.gov in this timeframe.**
229,503	(5,165)	466,621	(13,607)	Trials where patients were recruited
176,237	(53,266)	227,443	(239,178)	Trials with primary completion date after window start-date
138,186	(38,051)	169,439	(58,004)	Trials with interventional study design
118,652	(19,534)	150,454	(18,985)	Trials that were not phase 0 or phase 1
47,981	(70,671)	48,732	(101,722)	Trials that met pre-specified criteria for intervention or FDA oversight
24,042	(23,939)	21,934	(26,798)	Trials with "completed" or "terminated" recruitment status
15,033	(9,009)	10,399	(11,535)	Trials with primary completion date before window end date
14,174	(859)	9,880	(519)	For trials with missing primary completion date and completion date, check last verification date is within window start and end
14,174		**9,880**		**Trials considered to be highly likely applicable clinical trials (HLACTs)**

To validate our methodology, we compared our implementation of Anderson et al.'s algorithm against their original dataset.[10] Our analysis of trials classified as HLACTs closely matched their results, as detailed in section 5.1.

2.1 Definitions

Observational windows: Anderson et al.[7] looks at studies with completion dates from January 1, 2008 to September 1, 2012. This time frame is associated with a cut-off date of when the dataset was downloaded from ClinicalTrials.gov on September 27, 2013. These three dates define an observational window in which we can track the number of months after trial completion until a given trial has submitted their results.

In a similar manner, to evaluate compliance rates before and after the 2017 mandate, we constructed two equivalently sized windows. Window 1: trials completed between January 18th of 2010–2014, tracked until 2017. Window 2: trials completed between January 18th of 2017–2021, tracked until 2024.

To better understand the nature of this change over time, we additionally constructed annual windows from 2008–2009, ... 2020–2021, and track reporting rates for 36 months. All analyses were done without accounting for extensions, a supplemental analysis (fig. 11) is provided which performs the same analysis while accounting for extensions.

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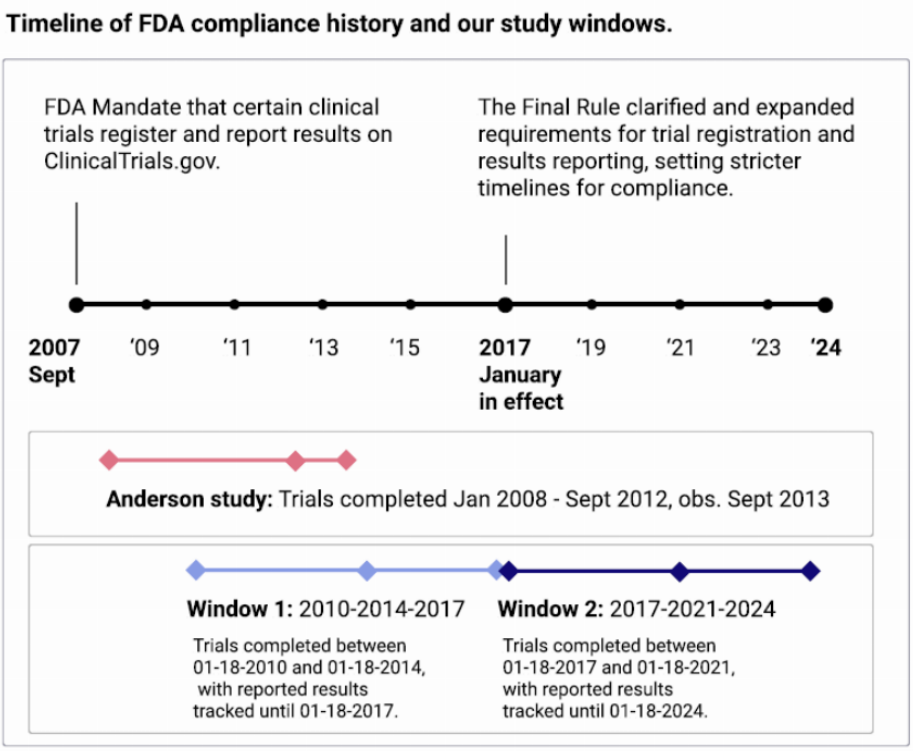
Timeline of FDA compliance history and our study windows.
FDA Mandate that certain clinical trials register and report results on ClinicalTrials.gov.
The Final Rule clarified and expanded requirements for trial registration and results reporting, setting stricter timelines for compliance.
2007 Sept
'09
'11
'13
'15
2017 January in effect
'19
'21
'23
'24
Anderson study: Trials completed Jan 2008 - Sept 2012, obs. Sept 2013
Window 1: 2010-2014-2017
Trials completed between 01-18-2010 and 01-18-2014, with reported results tracked until 01-18-2017.
Window 2: 2017-2021-2024
Trials completed between 01-18-2017 and 01-18-2021, with reported results tracked until 01-18-2024.

Figure 1: Timeline of FDAAA mandates, Anderson study, and our study windows. Observation windows 1 and 2 span 4 years, tracking results reported within 3 years.

The trial characteristics and their subgroups considered are:

Funding source: Industry, NIH, Other academic or government institution;

Trial phase: Phase 1/2, 2, Phase 2/3, 3, Phase 4, Phase N/A;

Intervention type: Drug, Biologic, Device, Other; and

Trial primary purpose: Treatment, Prevention, Other.

Trials funded from “Other” sources include government agencies, academic institutions, and nonprofit/private organizations. Trials with “N/A” phase may include diagnostics or devices that don’t follow the same progression as drug trials, or trials for expanded access or compassionate use that offer experimental therapies to patients outside of a traditional clinical trial setting.[11] Trials categorized as “Other” intervention types include trials for behavioral studies, procedures, or diagnostics. Trials categorized as having “Other” primary purpose include studies for educational/counseling/supportive care, screening, health services research.[12]

2.2 Data Sources

The ClinicalTrials.gov database allows investigators to modify trial information, including fields like start date and completion date, even after a trial has been completed. This ability to update metadata complicates the process of reproducing historical studies. To obtain data as close to that of [10], we used the ClinicalTrials.gov API to retrieve all

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versions of study records by their NCT numbers from the database[13] as of April 30, 2024. These records are stored in the form (NCTID, version, change-date, study-record), allowing us to retrieve the latest version of each record as it existed at our window's cut-off date. After filtering records by the cut-off date, the rest of the algorithm is applied as shown in section 5.1.1.

2.3 Statistical analysis

Rates of reporting within 12 months and reporting within 36 months are presented for HLACTs in Window 1 and Window 2, alongside the difference in rates between the windows. These analyses are also conducted across various subcategories and demonstrate differences between subcategories, as well as the percent change within each subcategory.

Kaplan-Meier survival curves show the cumulative percentage of trials that reported results from the completion date, and are stratified by sub-category and separated by windows. The slopes and magnitude of these curves serve as a more continuous way to understand rates of reporting over time, instead of a binary separation of "reporting within 12 months" and "reporting within 36 months."

A permutation test was conducted to assess the significance of the observed difference between the two groups. We report confidence intervals of the difference in proportion of trials reporting within 12 months between Window 2 and Window 1, as well as within 36 months.

3 - Results

3.1 Window 1 & Window 2 Rates of Reporting

Results show a +14.9% increase in trials reporting within 12 months, from 8.3% in Window 1 to 23.2% in Window 2. Reporting within 36 months increased by +8.5%, from 40.8% to 49.2%. Despite these improvements, a majority of trials in Window 2 remained out of compliance (76.8%), and roughly half (50.8%) did not report within 36 months (fig. 2). Similar patterns emerge when accounting for regulatory reporting extensions: Window 2 showed an +18% increase in 12-month reporting and an +8% increase in 36-month reporting compared to Window 1 (fig. 11).

Differences in compliance rates within stratified groups (fig. 3) show increased compliance across all subgroups, with variation.

Funding: In Window 2, both Industry and NIH-funded trials had nearly identical reportingrates, with 31.5% and 32.2% of trials reporting within 12 months respectively. By 36 months, Industry-funded trials had a slightly higher reporting rate compared to NIH-funded trials(67.1% vs. 62.0%). However, NIH-funded trials showed significant improvement from Window 1 to Window 2, with reporting rates increasing from 39.2% to 62.0%.

Intervention type: Biologics and Drugs have had much higher rates of timely reporting compared to Devices. In Window 2, reporting rates for Biologics at 12-months and 36-months were 45.3% and 85.2%, Drugs were 37.9% and 81.5%, and Devices were 30.0% and 64.0%, respectively. This may reflect strict regulatory oversight of pharmaceutical interventions, generally with more structured timelines and well-defined reporting requirements, whereas different device types have varying reporting requirements and often involve longer timelines that require iterative development.

Phase: Reporting rates are comparable across trial phases, with later phases having slightly higher rates.

Purpose: Treatment trials had higher rates of timely reporting than Prevention trials in both windows.

While primary categories saw improvements in timely reporting of approximately 20%, trials classified as 'Other' in their Funding, Intervention Type, or Purpose showed minimal change.

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When comparing compliance rates across Window 1 and 2, differences in trial type distributions in the two windows is something to consider. This topic is explored more in section 5.2.

Kaplan-Meier survival curves, stratified by funding source, reveal that industry and NIH-funded trials had very similar compliance rates in Window 2, in contrast to Window 1 (fig. 4). Trials funded by other government agencies and academic institutions showed no meaningful improvement in compliance between the windows. Additional Kaplan-Meier curves, illustrating trends by intervention type and trial phase, are presented in section 5.3.

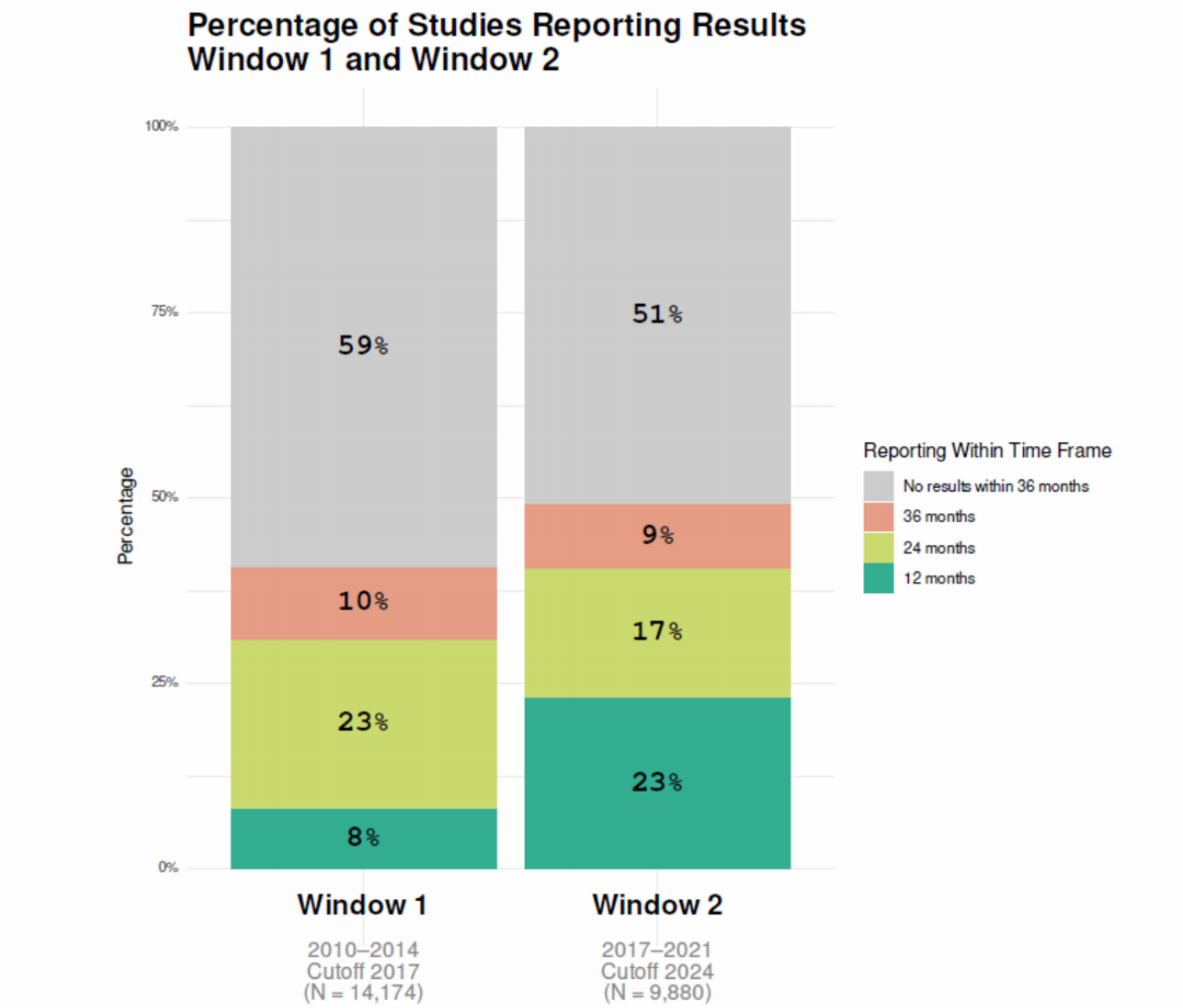

Figure 2: Results before and after the FDAAA Final Rule effective date.

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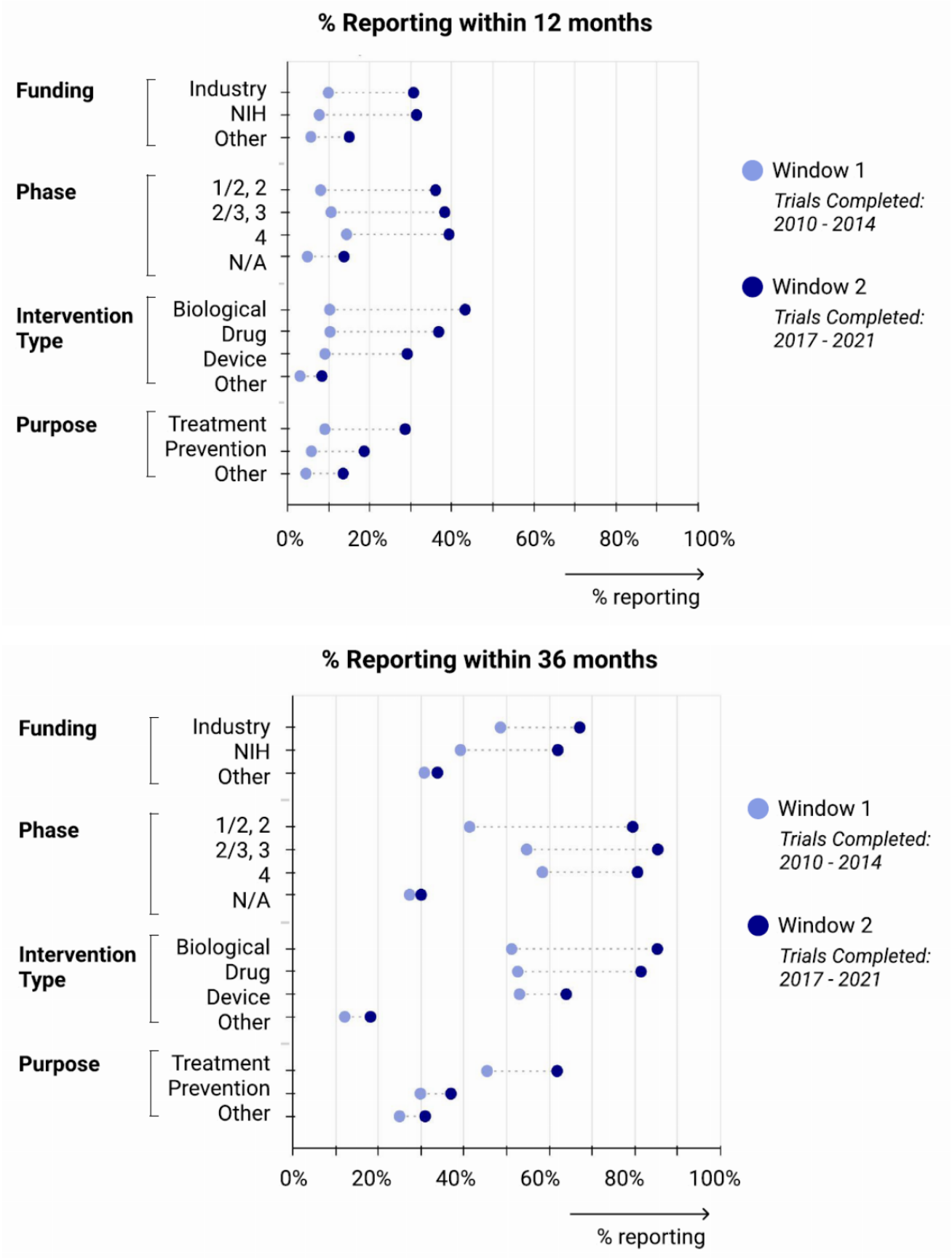

Figure 3: Rates of timely reporting amongst subgroups: Funding source, Trial phase, Intervention type, Trial purpose in Window 1 and Window 2. Section 5.4 shows source data.

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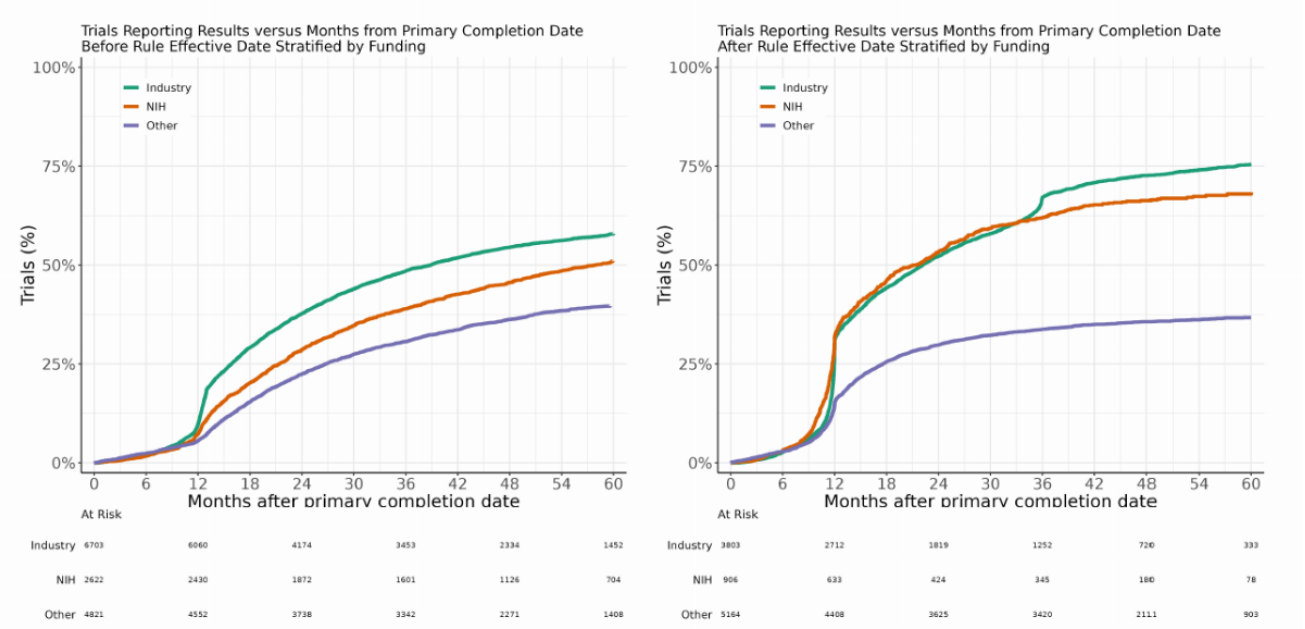
Trials Reporting Results versus Months from Primary Completion Date
Before Rule Effective Date Stratified by Funding
Trials Reporting Results versus Months from Primary Completion Date
After Rule Effective Date Stratified by Funding
Industry
NIH
Other
Trials (%)
100%
75%
50%
25%
0%
0 6 12 18 24 30 36 42 48 54 60
Months after primary completion date
At Risk
Industry 6703 6060 4174 3453 2334 1452
NIH 2622 2430 1872 1601 1126 704
Other 4821 4552 3738 3342 2271 1408
Industry 3803 2712 1819 1252 720 333
NIH 906 633 424 345 180 78
Other 5164 4408 3625 3420 2111 903

Figure 4: Cumulative percentage of clinical trials that reported results by time after primary completion date, stratified by funding source for Window 1 and Window 2. Numbers below each graph show count of trials remaining unreported at specified time points, with initial counts (leftmost column) representing total trials in each funding category.

3.2 Annual Windows: Rates of Reporting, Time to Report

Annual windows provide a more holistic view of compliance from 2008 to 2021. There has been a steady increase in timely reporting: 12-month reporting rates rose from 3.6% to 28.2% from the 2008–2009 window to the 2020–2021 window, and 36-month reporting rates increased from 24.4% to 55.2% over this period.

Compliance generally improved by 1–3% per year, except during 2015–2016, when the rate jumped from 13.6% to 21.0% (+7.4%). This coincides with Anderson's publication in 2015 and suggests anticipation of the FDAAA 2017 reporting mandate. Overall, reporting compliance has seen significant improvements, with 55.2% of trials now reporting within three years of completion (fig. 5(a)).

For trials that report within 36 months, the distribution of months to report has declined from roughly 13–25 months to 11–18 months (25th–75th percentile). The median has also steadily declined from 15 months to 12 months (fig. 5(b)). The proximity of the 25th and 50th percentiles post-2017 indicates that many trials are reporting very close to the deadline. Additionally, the total number of reporting trials has increased, demonstrating that not only is the median time decreasing, but more trials overall are reporting more quickly.

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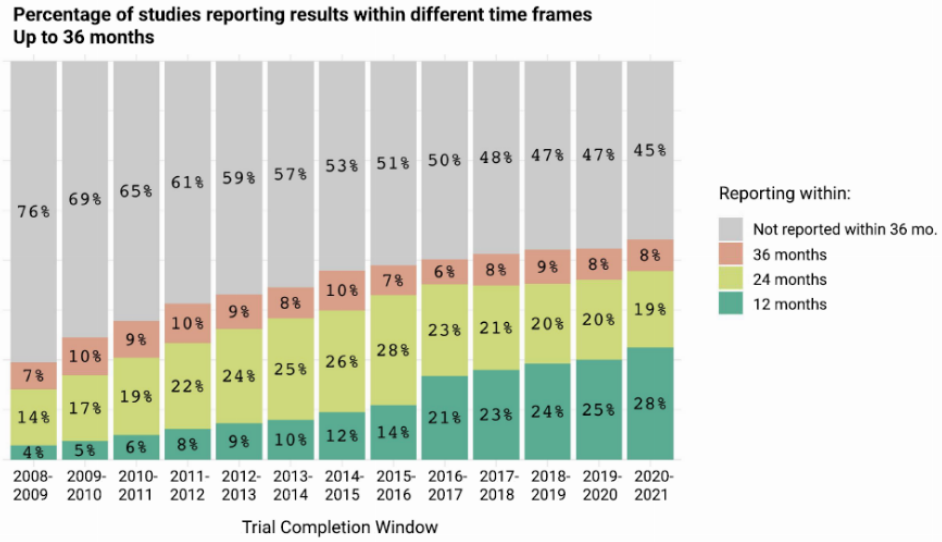
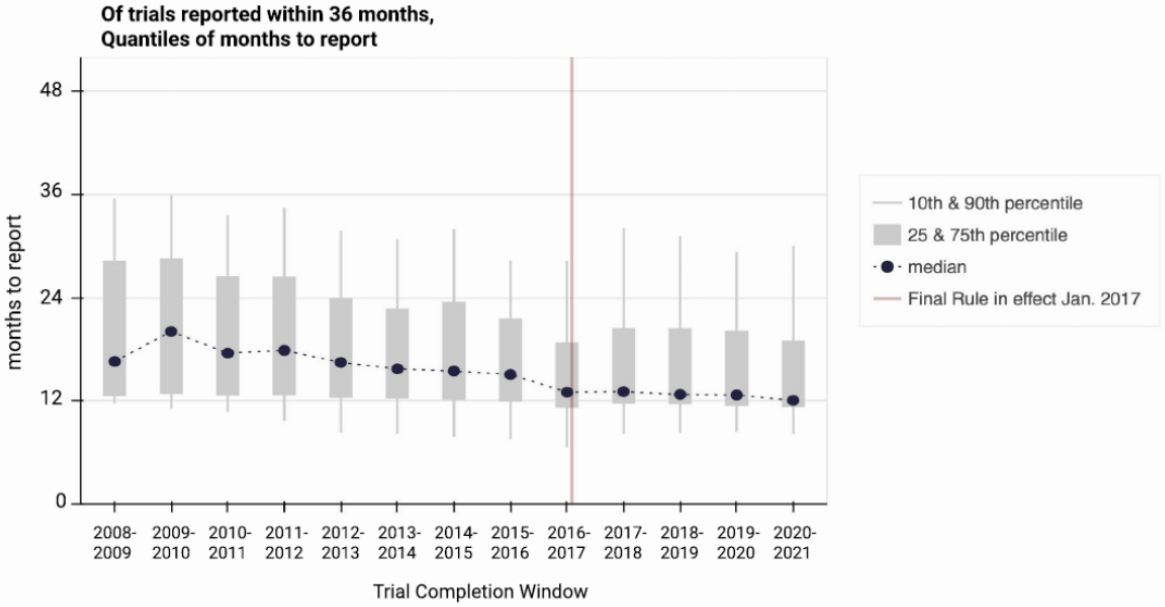


(a) Proportion of trials reporting results within 12, 24, and 36 months, as well as those not reporting within a three-year cutoff for each annual window.



(b) Distribution of months to report for trials reporting within 36 months.

Figure 5: Reporting rates for annual windows over 2008-2021. Note that to compare across years, we truncate the data at 36 months, otherwise trials completed in 2009 would have 15 years to report results, whereas trials in 2020 would have only 4 years, which would lead to misleading comparisons.

3.3 Statistical Analysis

A permutation test was performed to assess whether the observed differences between Window 1 (N=14,174) and Window 2 (N=9,880) reporting rates could have occurred by chance. The test repeatedly shuffles the window assignments randomly across trials and recalculates the difference in reporting rates. The p-value represents the proportion of permutations that produce a difference as extreme as or more extreme than the observed difference. For both the 12-month and 36-month reporting rates, p-values less than 0.001 were obtained, indicating that the probability of observing such large differences between windows due to random chance is extremely small. This provides strong statistical evidence that the improvements in reporting rates between Window 1 and Window 2 (12

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months: +14.9%, 36 months: +8.5%) represent genuine changes in trial reporting behavior. These findings are consistent across all stratified subcategories (table 4).

4 - Discussion

The history of reporting requirements for clinical trial results reflects a long-standing need for transparency in research involving human subjects. ClinicalTrials.gov, established by Congress in 2000, was envisioned as a centralized resource for information and results data on clinical trials; however, it was the Food and Drug Administration Amendments Act (FDAAA) of 2007 that introduced the regulatory framework requiring the formal reporting of trial results. Under FDAAA 801, sponsors of applicable clinical trials (ACTs) were required to submit summary results within a year of trial completion. Compliance with these regulations became enforceable through the FDAAA 2017 Final Rule, which introduced penalties for non-compliance, including fines, the potential loss of federal funding, and public disclosure of non-compliance. This change was a significant regulatory step aimed at improving transparency and accountability in clinical research.

Prior to the 2017 mandate, compliance was low, with only 13.4% of trials reporting results within 12 months.[7] Our analysis shows a marked improvement, with timely reporting increasing from 8.3% (2010–2014) to 23.2% (2017–2021). Reporting within 36 months also rose, from 40.8% to 49.2%. Compliance varied across trial types, with device trials lagging behind drugs and biologics. Industry- and NIH-funded trials now report at similar rates, reflecting the impact of penalties like loss of federal funding. Limitations of our study include not knowing which trials have requested and been granted extensions, the ability of studies to modify their completion dates, and the likely preponderance of studies which remain “open” despite internal decisions to discontinue. However, these analyses suggest that the 2017 mandate has positively influenced reporting practices, even if compliance rates are still far from ideal.

There are various documented reasons why trials still struggle to report results on time. In 2022, the Clinical Trials Transformation Initiative (CTTI) conducted 26 interviews with investigators and sponsors of applicable trials, aiming to identify specific challenges they face. The report[14] identified gaps in clinician understanding of which trials require registration and when to submit results. This further indicates the need for communication and trial reporting tools to support and ease the process of trial reporting. Some sponsors are hesitant to post results, particularly if the trial outcomes are negative or inconclusive, due to reputational impact or future funding risks. Additionally, the reporting process itself can be complex and time-consuming, with researchers citing technical difficulties, issues with data entry, and unclear guidance as barriers. Academic institutions, in particular, often lack the resources and specialized staff required to meet stringent reporting timelines compared to industry sponsors.

The challenge of timely reporting should also not be viewed solely as a compliance issue. Clinical researchers face significant practical hurdles in meeting reporting requirements, including the need to ensure HIPAA compliance when handling patient data and the substantial time investment required to format and input data into ClinicalTrials.gov’s system. Rather than focusing on enforcement alone, developing better computational tools and systems to support efficient, compliant FAIR data submission could help improve reporting rates. Such tools could automate parts of the submission process, provide clear guidance on reporting requirements, and help ensure data quality while reducing the administrative burden on clinical research teams.

In summary, our findings indicate that compliance rates have improved since the 2017 FDAAA Final Rule mandate, with more trials reporting results within 12 and 36 months of completion. This increase in compliance has been influenced by a combination of regulatory, institutional, and societal factors. The 2017 FDAAA Final Rule introduced enforcement mechanisms, including financial penalties and public accountability, although the potential $10,000/day fine is seldom levied. There have been efforts on the part of NIH to enhance technological tools and simplify reporting processes via more user-friendly submission platforms and automated reminders. Evolving institutional policies and shifts toward reproducibility in research practices, including federal mandates, internal ethical standards, and international harmonization contribute to increased compliance. Public advocacy campaigns and media scrutiny have heightened awareness and pressured organizations to prioritize transparency. Together, these elements have created a slightly more robust framework for supporting timely and accurate reporting of clinical trial results. Despite these improvements, a majority of trials still remain out of compliance, with around 50% failing to report within three years. To address this ongoing challenge, public tracking tools like the FDAAA TrialsTracker have emerged to monitor compliance in real-time and support accountability. These tools not only help regulators identify non-compliant trials but also assist sponsors in tracking their own reporting obligations, potentially serving as a practical solution to improve overall compliance rates.

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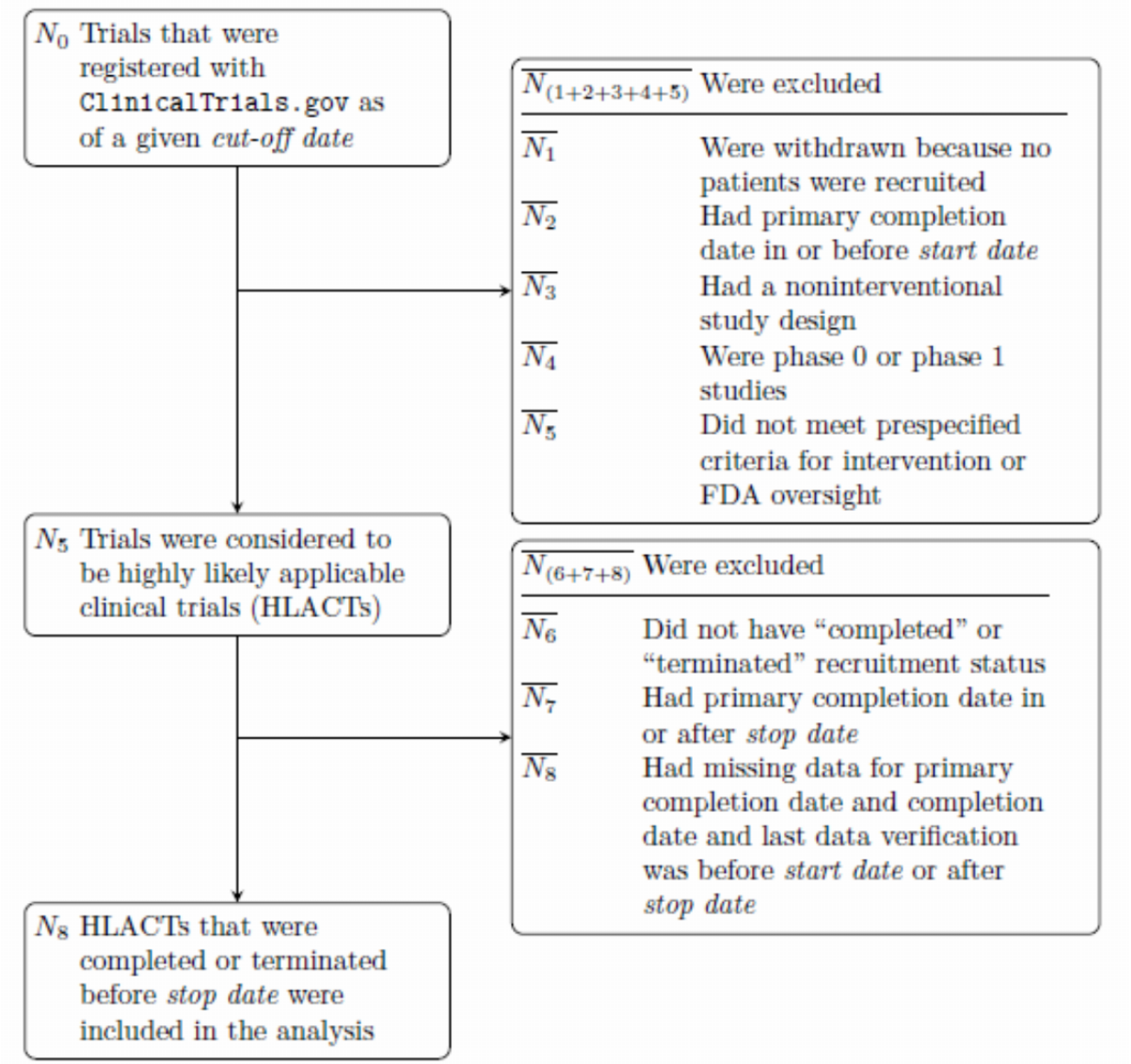
Beyond the obvious enforcement actions, addressing these root causes could help further boost compliance rates. For example, simplifying the user interface on ClinicalTrials.gov, providing more robust support for academic researchers, or revising publication-related restrictions could remove barriers and encourage more rapid reporting. With the advent of artificial intelligence and continuously improving computational modeling capabilities, comprehensive access to data becomes even more critical to support generation of large-scale knowledge networks that will yield insights into human disease. Facilitating timely reporting of clinical trial results is not only a regulatory obligation but also an ethical imperative, essential to advancing medical knowledge, ensuring public trust, and ultimately improving patient outcomes.

For full reproducibility, project code and methodologies are available at https://github.com/insilica/clinicaltrials-compliance-study.

5 - Supplement

5.1 Replicating Anderson Methodology

Figure 6: Flowchart determining the HLACTs for a given window.


N_0 Trials that were registered with ClinicalTrials.gov as of a given *cut-off date*
$\overline{N_{(1+2+3+4+5)}}$ Were excluded
$\overline{N_1}$ Were withdrawn because no patients were recruited
$\overline{N_2}$ Had primary completion date in or before *start date*
$\overline{N_3}$ Had a noninterventional study design
$\overline{N_4}$ Were phase 0 or phase 1 studies
$\overline{N_5}$ Did not meet prespecified criteria for intervention or FDA oversight
N_5 Trials were considered to be highly likely applicable clinical trials (HLACTs)
$\overline{N_{(6+7+8)}}$ Were excluded
$\overline{N_6}$ Did not have "completed" or "terminated" recruitment status
$\overline{N_7}$ Had primary completion date in or after *stop date*
$\overline{N_8}$ Had missing data for primary completion date and completion date and last data verification was before *start date* or after *stop date*
N_8 HLACTs that were completed or terminated before *stop date* were included in the analysis

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5.1.1 Algorithm for Funding Source

Algorithm 1 Pseudocode to Normalize Funding Source: Each study has a derived *funding source* variable which is defined by normalizing the `ClinicalTrials.gov` data elements of the lead sponsor class and any collaborator classes.

```
function NORMALIZE_FUNDING_SOURCE(lead_sponsor_funding_source: String, collaborators_classes: List of Strings)
    if lead_sponsor_funding_source = 'NIH' then
        return 'NIH'
    else if 'NIH' ∈ collaborators_classes and lead_sponsor_funding_source ≠ 'INDUSTRY' then
        return 'NIH'
    else if lead_sponsor_funding_source = 'INDUSTRY' then
        return 'Industry'
    else if 'INDUSTRY' ∈ collaborators_classes then
        return 'Industry'
    else
        return 'Other'
    end if
end function
```

5.1.2 Recreating Table 1 — our algorithm with Anderson data

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Characteristic	All trials N = 13,327[1]	Results Report by 12 Mo N = 1,803[1]	Results Report by 5 Yr N = 5,095[1]
Primary Purpose			
Treatment	10,930 (85%)	1,519 (87%)	4,231 (86%)
Prevention	990 (7.7%)	134 (7.7%)	392 (7.9%)
Other	964 (7.5%)	95 (5.4%)	316 (6.4%)
Unknown	443	55	156
Intervention Type			
Drug	10,309 (77%)	1,423 (79%)	3,981 (78%)
Biological	1,185 (8.9%)	170 (9.4%)	491 (9.6%)
Device	1,586 (12%)	198 (11%)	578 (11%)
Other	247 (1.9%)	12 (0.7%)	45 (0.9%)
Phase Type			
1-2	867 (6.5%)	65 (3.6%)	238 (4.7%)
2	4,917 (37%)	470 (26%)	1,627 (32%)
2-3	333 (2.5%)	20 (1.1%)	105 (2.1%)
3	3,117 (23%)	654 (36%)	1,509 (30%)
4	1,928 (14%)	393 (22%)	915 (18%)
Not applicable	2,165 (16%)	201 (11%)	701 (14%)
Funding Type			
Industry	8,736 (66%)	1,491 (83%)	3,612 (71%)
NIH	1,899 (14%)	157 (8.7%)	738 (14%)
Other	2,692 (20%)	155 (8.6%)	745 (15%)
Completed Year			
2008	3,142 (24%)	370 (21%)	1,357 (27%)
2009	3,051 (23%)	373 (21%)	1,407 (28%)
2010	2,853 (21%)	408 (23%)	1,154 (23%)
2011	2,686 (20%)	420 (23%)	888 (17%)
2012	1,595 (12%)	232 (13%)	289 (5.7%)

[1] n (%)

5.1.3 Survival Curves Comparison

Figure 7: Survival stratified by various variables using Anderson et al.[10]

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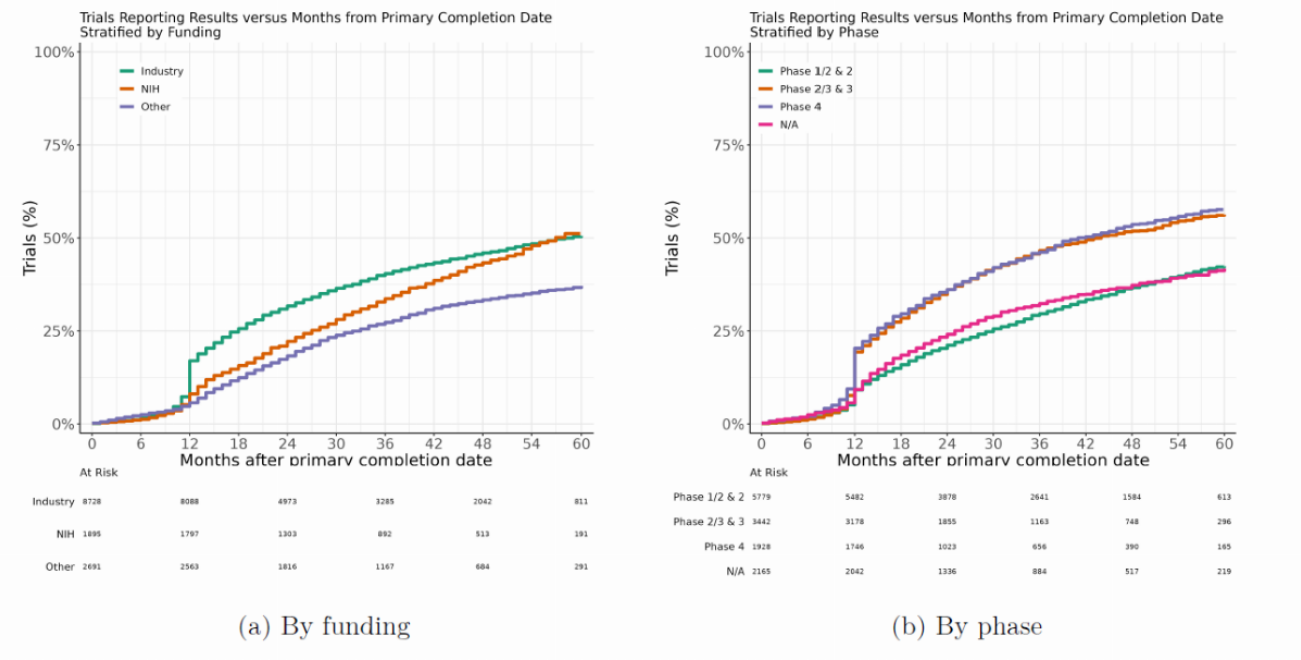
Trials Reporting Results versus Months from Primary Completion Date
Stratified by Funding
Industry
NIH
Other
Trials (%)
Months after primary completion date
At Risk
Industry 8728 8088 4973 3285 2042 811
NIH 1895 1797 1303 892 513 191
Other 2691 2563 1816 1167 684 291
(a) By funding
Trials Reporting Results versus Months from Primary Completion Date
Stratified by Phase
Phase 1/2 & 2
Phase 2/3 & 3
Phase 4
N/A
Trials (%)
Months after primary completion date
At Risk
Phase 1/2 & 2 5779 5482 3878 2641 1584 613
Phase 2/3 & 3 3442 3178 1855 1163 748 296
Phase 4 1928 1746 1023 656 390 165
N/A 2165 2042 1336 884 517 219
(b) By phase
Trials Reporting Results versus Months from Primary Completion Date
Stratified by Intervention Type
Device
Biological
Drug
Other
Trials (%)
Months after primary completion date
At Risk
Device 1586 1470 895 566 311 124
Biological 1183 1104 706 430 217 85
Drug 10298 9635 6310 4226 2639 1053
Other 247 239 181 122 72 31
(c) By interventions
Trials Reporting Results versus Months from Primary Completion Date
Stratified by Terminated/Completed Status
Completed
Terminated
Trials (%)
Months after primary completion date
At Risk
Completed 11116 10413 6741 4475 2709 1107
Terminated 2198 2035 1351 869 530 186
(d) By status

Table 3: Windows comparing before and after rule-effective date. Observation windows span 4 years, tacking results reported within 3 years.

Name	Start	Stop	Cut-off
Before (Window 1)	2010-01-18	2014-01-18	2017-01-18
After (Window 2)	2017-01-18	2021-01-18	2024-01-18

5.2 Trial Type Composition changes between Window 1 and Window 2

Differences in trial type distribution is something to consider before comparing compliance rates between Window 1 and 2. Figure 8(a) shows the breakdown of subcategories for our entire sample, and highlights the proportion of Other/NA values present. Figure 8(b) shows the % change in

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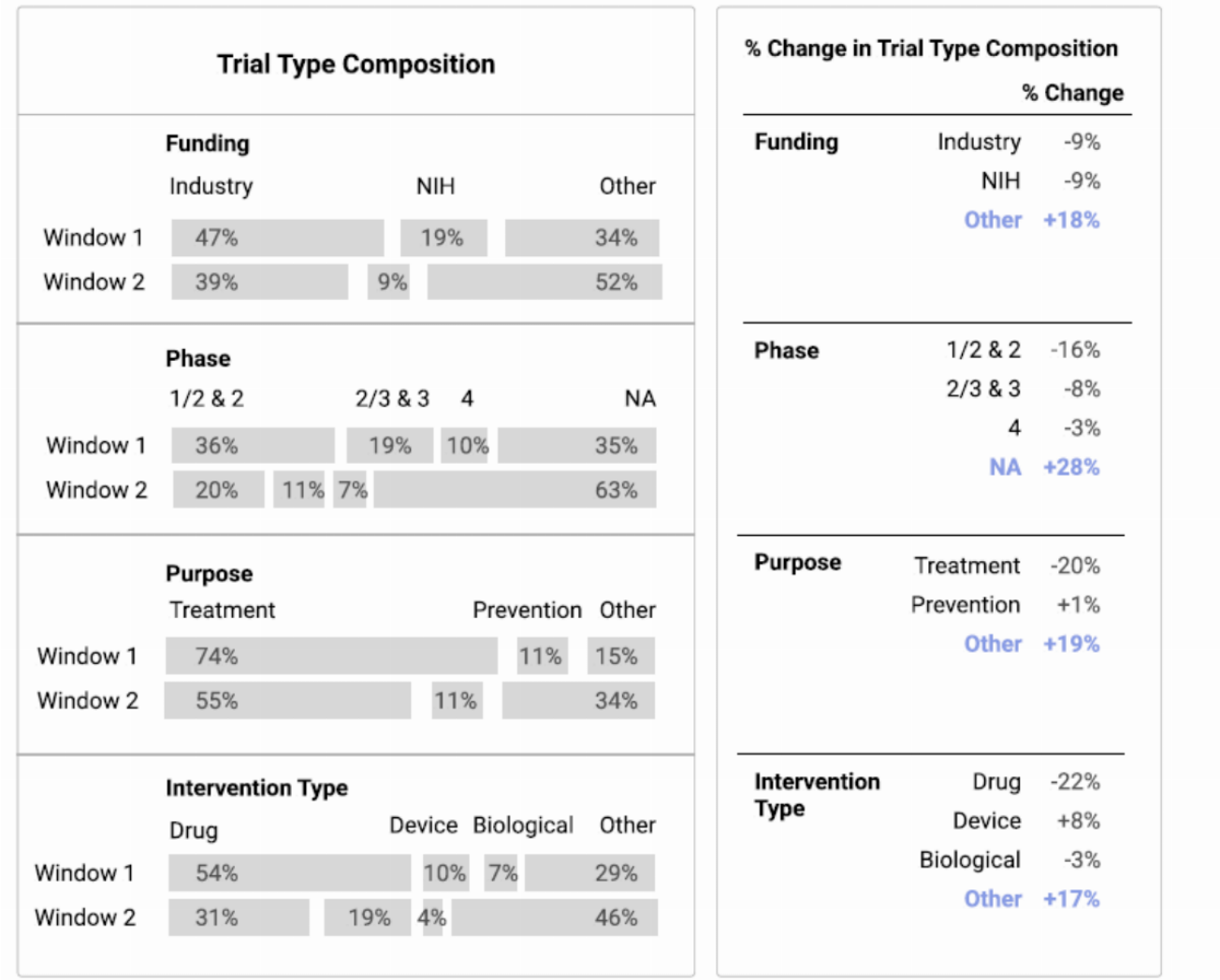
categories across the two observation windows. For example, industry-funded trials made up 47.4% of trials in Window 1, and 38.5% of trials in Window 2, for a difference of −8.9%. This allows us to roughly approximate the sample sizes of each subcategory, and consider the underlying trial type shifts over this time period.

Figure 8 : Trial Type Composition changes between Window 1 and Window 2



(a) Composition of trial population

(b) Percent change in trial population composition

5.3 Additional Survival Curves by Trial Characteristics in Window 1, Window 2

Figure 9: Cumulative percentage of clinical trials that reported results by time after primary completion date stratified by *phase* for the windows in table 3.

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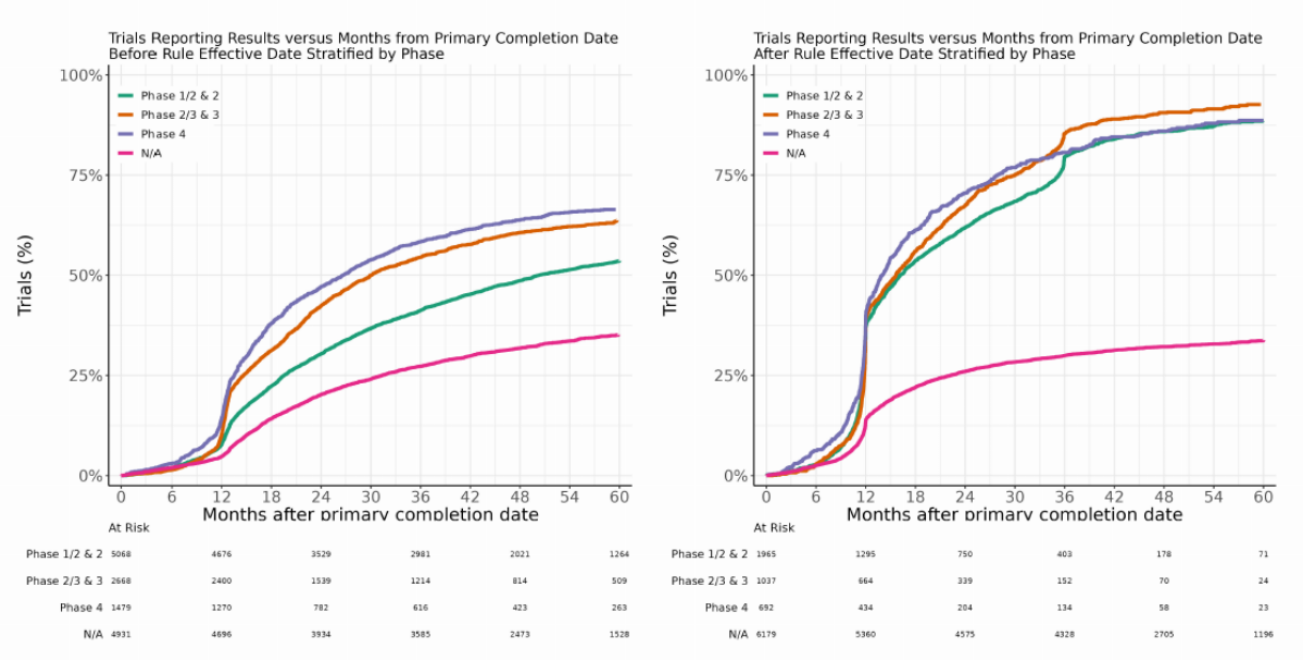
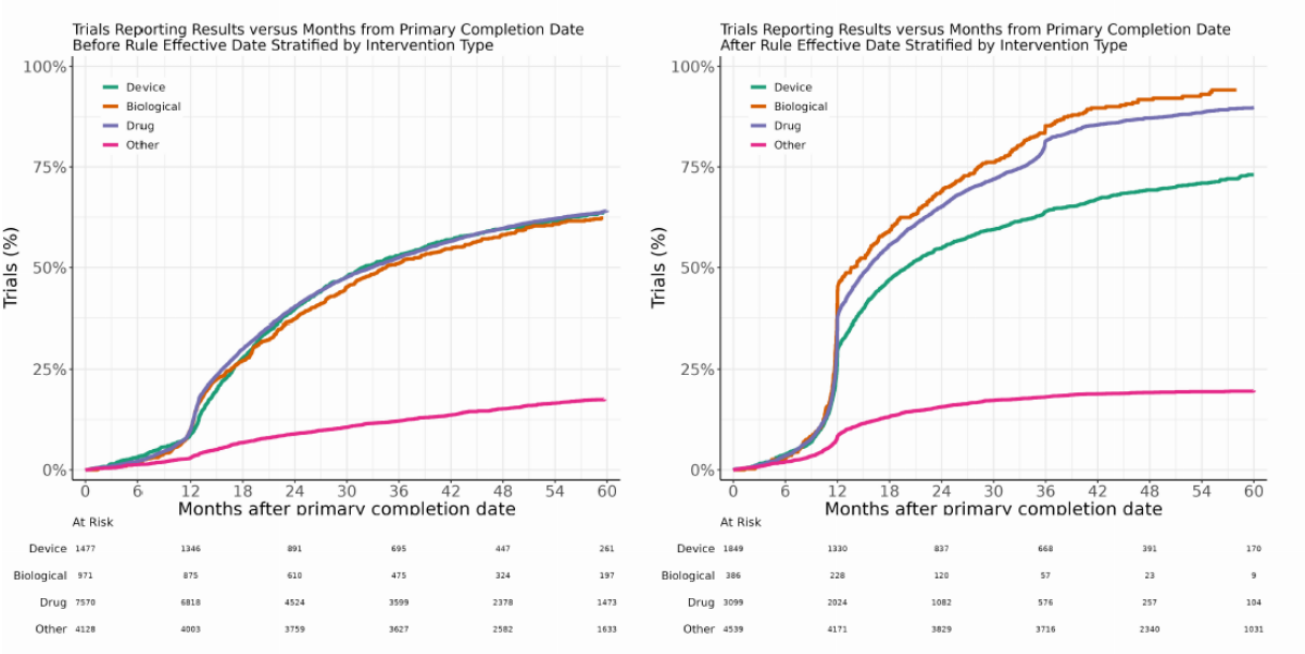

Trials Reporting Results versus Months from Primary Completion Date
Before Rule Effective Date Stratified by Phase
Trials Reporting Results versus Months from Primary Completion Date
After Rule Effective Date Stratified by Phase
Phase 1/2 & 2
Phase 2/3 & 3
Phase 4
N/A
Trials (%)
100%
75%
50%
25%
0%
0 6 12 18 24 30 36 42 48 54 60
Months after primary completion date
At Risk
Phase 1/2 & 2 5068 4676 3529 2981 2021 1264
Phase 2/3 & 3 2668 2400 1539 1214 814 509
Phase 4 1479 1270 782 616 423 263
N/A 4931 4696 3934 3585 2473 1528
Phase 1/2 & 2 1965 1295 750 403 178 71
Phase 2/3 & 3 1037 664 339 152 70 24
Phase 4 692 434 204 134 58 23
N/A 6179 5360 4575 4328 2705 1196

Figure 10: Cumulative percentage of clinical trials that reported results by time after primary completion date stratified by *intervention type* for the windows in table 3.


Trials Reporting Results versus Months from Primary Completion Date
Before Rule Effective Date Stratified by Intervention Type
Trials Reporting Results versus Months from Primary Completion Date
After Rule Effective Date Stratified by Intervention Type
Device
Biological
Drug
Other
Trials (%)
100%
75%
50%
25%
0%
0 6 12 18 24 30 36 42 48 54 60
Months after primary completion date
At Risk
Device 1477 1346 891 695 447 261
Biological 971 875 610 475 324 197
Drug 7570 6818 4524 3599 2378 1473
Other 4128 4003 3759 3627 2582 1633
Device 1849 1330 837 668 391 170
Biological 386 228 120 57 23 9
Drug 3099 2024 1082 576 257 104
Other 4539 4171 3829 3716 2340 1031

5.4 Table of Trial Characteristic Months to Report

Table 4: Permutation test results at (N = 50,000 replicates), stratified by Trial Characteristics

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Group		12-month Results				36-month Results			
	Subgroup	Pre (%)	Post (%)	Δ (%)	p-value	Pre (%)	Post (%)	Δ (%)	p-value
Funding	NIH	7.8	32.2	+24.4	0.0	39.2	62.0	+22.7	0.0
	Industry	10.2	31.5	+21.3	0.0	48.6	67.1	+18.5	0.0
	Other	5.8	15.5	+9.8	0.0	30.8	33.8	+3.1	8.0E−4
Phase	Phase 1/2 & 2	8.2	37.3	+29.1	0.0	41.4	79.6	+38.1	0.0
	Phase 2/3 & 3	11.0	39.3	+28.3	0.0	54.7	85.4	+30.7	0.0
	Phase 4	14.6	40.5	+25.9	0.0	58.4	80.6	+22.3	0.0
	N/A	4.9	14.1	+9.2	0.0	27.3	30.0	+2.7	1.2E−3
Intervention	Drug	10.6	37.9	+27.3	0.0	52.6	81.5	+28.8	0.0
	Device	9.1	30.0	+20.8	0.0	53.1	64.0	+10.9	0.0
	Biological	10.7	45.3	+34.6	0.0	51.2	85.2	+34.1	0.0
	Other	3.1	8.5	+5.4	0.0	12.2	18.2	+6.0	0.0
Purpose	Treatment	9.3	29.5	+20.2	0.0	45.5	61.8	+16.4	0.0
	Prevention	5.9	19.0	+13.1	0.0	29.9	37.0	+7.1	6.0E−5
	Diagnostic	5.6	19.9	+14.2	0.0	37.7	52.0	+14.3	4.0E−5
	Other	4.6	13.9	+9.4	0.0	25.0	31.0	+6.0	2.0E−5

5.5 Confidence Intervals of % Change in Reporting from Window 1 to Window 2

Although the dataset theoretically includes all applicable trials, confidence intervals were calculated to account for potential classification errors introduced by the algorithm for identifying trials. These intervals help assess the robustness of the findings regarding changes in reporting rates between Window 1 and Window 2:

The improvement in reporting within 12 months was +14.9% (95% CI: +14.0%, +15.9%). The increase in reporting within 36 months was +8.4% (95% CI: +7.2%, +9.7%).

6 - Reporting results compared when accounting for extensions

When trials are given a certification to delay results, per §11.44(b)(2) of the regulation, they are given two years from the date of the certificate submission to submit the result information. To provide a comparable time interval from trial completion to result submission as in the standard deadline trials, this is equivalent to computing the interval to the result submission date from the certification submission date plus one year.

Figure 11: Results before and after the FDAAA Final Rule effective date when accounting for extensions.

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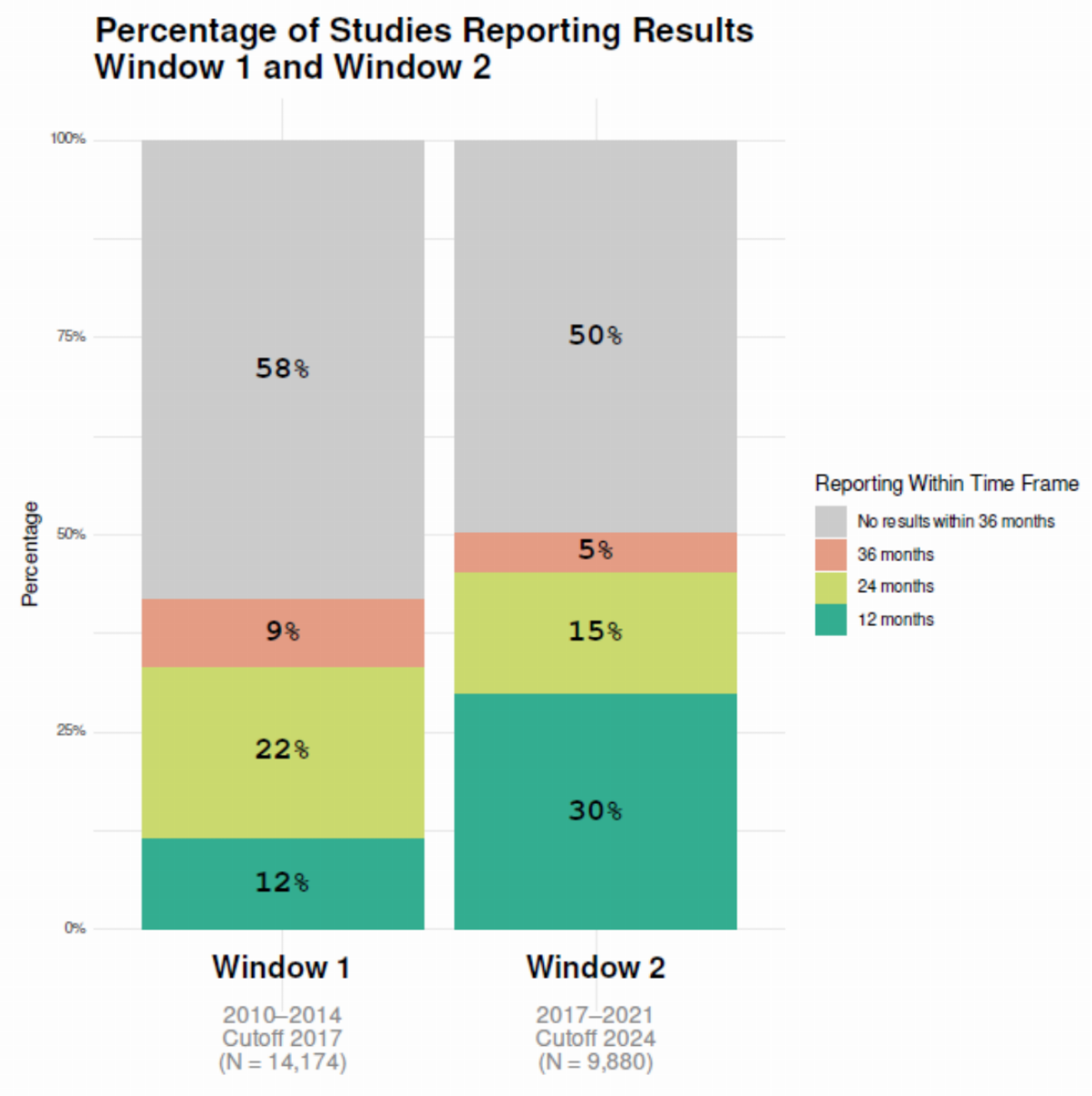

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Peer Review of: Compliance with Results Reporting at ClinicalTrials.gov Before and After the 2017 FDAAA Final Rule: A Comparative Analysis

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DOI: https://doi.org/10.70542/rcj-japh-pr-16w21ul

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In general, I find the manuscript to be well written and clear. The authors replicate methodology from the study by Anderson et al assessing researcher compliance in reporting data from clinical trials as mandated by the updated 2017 FDAAA Final Rule. The rationale for the current study is to assess if compliance had improved since the Anderson report and the 2017 FDAAA Final Rule.

The authors indeed perform a comprehensive analysis, including pre- and post- assessments in aggregate for the time spans covered as well as annually. They also perform several important sensitivity analyses, selecting for funding source, Trial Phase, drug or device trial and trial primary purpose. They also assessed compliance withing 12- and 36-month time frames. Finally, in a supplemental analysis, they repurposed all these assessments for studies that were granted extensions.

The Results generally show an improvement in compliance with reporting requirements since the Updated Rule and the Anderson publication across in the primary analysis and the sensitivity analyses as well. Somewhat disappointingly but not unexpectedly, even though compliance rates improved, the rates were about 25% at 12 months and 50% at 36 months. Compliance rates were far better for industry sponsored trials.

The Discussion is appropriate and supported by the data in the Results. The authors' comments are free from overt speculation or bias.

My main concerns for the manuscript center around incomplete reporting of statistical analyses or results, with a reliance on subjective rather than objective measures of differences between the groups. In addition, I have several minor comments regarding the structure and reporting in the manuscript. These concerns are highlighted individually below by the manuscript section and not by order of importance.

Abstract

1. HLACT should be spelled out in this first instance.
2. The 95%CIs should be presented for all rates.

Methods

1. The choice of using the permutation test as the primary comparison is acceptable, but this test is usually performed when the sample sizes are small, which is not the case with this study. Furthermore, the authors do not state the number of shuffles that were performed (usually this is between 1000 to 10,000), which is standard when using the permutation test. Finally, the permutation test is usually used when prior rates are unknown, yet the Anderson paper provides these prior rates. Other non-parametric tests should have been considered.
2. The authors do not provide a level for significance in the Methods, nor do they report the statistical package used, both of which are common practice in medical reporting.
3. The authors do not compare the Kaplan Meier curves in each of the analyses, which is possible by long-rank test.

Results

1. The authors also provide several Kaplan-Meier graphs to provide a visual comparison of reporting compliance rates between different cohorts in the sensitivity analyses. In the Results, the authors use

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vague terms such as “generally improved”, “much higher rates” and “increased”, “significant improvement”, without any statistical comparison. Kaplan Meier curves can be compared statistically for objective differences using the log-rank test.

2. The authors have instances of data interpretation in the Results that should be left for the Discussion.

a. “This may reflect strict regulatory oversight of pharmaceutical interventions, generally with more structured timelines and well-defined reporting requirements, whereas different device types have varying reporting requirements and often involve longer timelines that require iterative development.

b. “This provides strong statistical evidence that the improvements in reporting rates between Window 1 and Window 2 (12 months: +14.9%, 36 months: +8.5%) represent genuine changes in trial reporting behavior.”

3. The 95%CI should be provided for all rates in every instance.

4. No need to have a “+” sign when the text states and increase.

5. Some of the numbers don’t match when added in the Results. For example, 40.8% + 8.5% doesn’t add up to 49.2%.

6. Some of the rates have one significant digit and others have none.

Discussion

1. The discussion is appropriate and not biased or speculative. It would have been interesting for the authors to have assessed whether there was a reporting bias against negative trials. I realize this is out of the scope of the current manuscript, but the authors could have cited literature that would support such a speculation.

Peer Review of: Compliance with Results Reporting at ClinicalTrials.gov Before and After the 2017 FDAAA Final Rule: A Comparative Analysis

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DOI: https://doi.org/10.70542/rcj-japh-pr-1dlyc48

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Mughal et al have conducted an analysis of reporting compliance in clinicaltrials.gov before and after the FDAAA. The analysis compares two time windows that are both 4 years in duration. The analysis finds that the FDAAA was associated with an increase in 12-month and 36 reporting rates.

Overall, this is a timely article about an important issue for physicians, scientists, and patients alike.

Major Critiques:

1. The selection of windows and time for follow-up is rational, but this is not well described in the Methods. A Figure in the Supplement might be useful to illustrate this decision and follow-up.

2. It is surprising that window 1 had more HLACTs than window 2. Is there a reason for this? Why is this the case? How can you be certain there is not ascertainment bias in the way studies were selected to account for this difference?

3. In the statistics section, which permutation test was done – and why was test selected – more information should be included

4. Section 3.3 should be renamed – statistical analysis should not be in the Results.

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5. Discussion – the order of the discussion is non-standard. The standard approach is:

a. The findings from this analysis
b. What others have shown
c. Significance of the previous and current findings d. Strengths
e. Limitations
f. Summary

While this recommendation is stylistic, I believe that this will enhance the flow of these interesting findings.

6. Figure 4 – seems odd that the 'other' category got worse – this should be commented on in the Discussion.

Minor Critiques:

Abstract

1. The acronym HLACT appears to be utilized without first having it written out.

2. The use of a reference in the abstract is non-standard and the entire sentence presumes information which has not yet been introduced. This should be corrected/modified.
3. The term 'consistent majority' is non-standard.
4. The second sentence of the conclusions is confusing and needs to be re-written.

5. Figure 1, Anderson study should have a footnote
6. 5.1.1 What is pseudocode?

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